knowhow on biocides to the participants from other developing countries and to set up an exchange of information and active strains.

These training activities, when carefully planned with detailed laboratory protocols made available to the participants, are important in encouraging them to attempt these experiments in their own laboratories. Thus a change in direction can only be brought about by practising and not by preaching.

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PERSPECTIVE

Reminiscences of the Recombinant DNA Story: Cloning the Gene for Luciferase

DeWitt Stetten, Jr., with the collaboration of William Gartland, and Bernard Talbot

The Recombinant DNA Molecule Program Advisory Committee discovered shortly after promulgation of the guidelines that the strict application thereof frequently led to preposterous results. Errors of judgement, inconsistencies, and legalistic defects seriously compromised the usefulness of the guidelines, as the following story will reveal.

In 1976, an application accompanied by a Memorandum of Understanding and Agreement was received from Marlene DeLuca who worked in the laboratory of William D. McElroy in San Diego. Members of this laboratory had long been concerned with problems of bioluminescence and specifically with the reactions that occur in the lantern of the common firefly. Whereas originally small urchins could be retained to deliver fireflies for mere pennies, inflation had now taken its toll so that the funds available to the laboratory were being eroded by the increasing cost of fireflies. DeLuca therefore quite appropriately proposed that the gene for the enzyme luciferase could readily be cloned in a suitable host-vector system to provide an inexpensive source of this valuable enzyme. Luciferase in the presence of luciferin and ATP will yield a flash of light which is easily measured, thus providing a simple, highly specific, and extraordinarily sensitive analytical method for assigning ATP concentrations. The guidelines at that time provided that experiments with insect DNA be performed under P3 containment, a level not available to the San Diego scientists. The guidelines did provide, however, that for insects which were not known to harbor any pathogenic agents, P2 containment might be substituted, provided the insects had been bred for ten generations under laboratory conditions, a period sufficient to dilute out any viral contaminants. In fact, fireflies had been handled for many years and in vast numbers, and there was no report anywhere of any disease related to or borne by any species of firefly. On the other hand, despite many attempts, no one had ever been able to get the firefly to reproduce under laboratory conditions. The life-cycle of this beetle takes two years, and on that basis alone it seemed unlikely that anyone would have taken the trouble to breed it in the laboratory for ten generations. Since no one, even in their wildest imaginings, could dream up a scenario whereby this experiment had any important elements of hazard, DeLuca requested that an exception be made permitting her to proceed with the isolation of luciferase DNA and its ultimate cloning under P2 conditions. The Committee gave this request its full attention. Its members were unable to devise any adverse scenarios. It approved enthusiastically the purpose of the proposed experiments and voted unanimously in its support. Possibly one of the reasons for the Committee's enthusiasm was the pleasing image which the application generated of our friend Bill McElroy, preferably dressed in a nightshirt and nightcap, surreptiously sneaking into his laboratory at midnight in the dark of the moon, pouring a few drops of luciferin solution and ATP solution on to each of his Petri plates, and collecting those colonies which glowed in the dark.

At this point a problem developed. The NIH administration ruled that what we had been calling guidelines were inflexible and therefore in effect 'regulations'. Since the guidelines did not state that exceptions could be granted, the NIH Director ruled that exceptions would not be granted until the guidelines were formally revised. Despite the fact that a number of legally trained persons had been overseeing the activities of our Committee, no one had warned us of this complication. We appealed to the Director, NIH, that a specific exception be granted in the present case in view of the absence of all likely hazards and the usefulness of the anticipated experimental result. The exception, however, was not forthcoming. We therefore had to advise our San Diego colleagues that permission to do the experiment, although unanimously supported by the Committee, had to be denied.

It was a few weeks later that I learned, to my amazement, that the premise upon which the particular guideline section was based (i.e. the concept that breeding insects for ten generations in the laboratory should dilute out viral contaminants) was itself false. Leon Rosen, a gifted virologist attached to the Public Health Service and stationed in Honolulu, reported that in the mosquito infected with dengue virus, viral particles were transmitted to the offspring due to their inclusion in the ova. We should have known about this defect in our logic, since the present observation was not the first observation of transmission of arboviruses from generation to generation in the mosquito and in the tick.

So we found ourselves trapped in an absurd quandary. We were denying to an excellently prepared laboratory permission to perform an experiment in which no one could visualize any hazard whatsoever. Because of a provision written into our guidelines, built on a premise proven untrue for a number of insect–virus associations, we were depriving the scientific community of the benefits that the experiment promised to

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yield. There appeared to be no escape from this quandary unless and until the guidelines were revised, an activity that was not completed until December 1978. Because of my growing feeling that we were doing the wrong things in the wrong way at the wrong time, I requested the Director, NIH, to find a new Chairman of the Recombinant DNA Molecule Program Advisory Committee to replace me, and was delighted when he accepted my nomination of Jane Setlow for this post. By virtue of her great patience and intelligence, she managed to hold the Committee on its track for the next two years.

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SCIENCE AND SOCIETY

Should Medical Research be Made a Criminal Act?

Peter R. Braude, Martin H. Johnson and Hester P. M. Pratt

In July of this year the report of the Committee of Inquiry into Human Fertilization and Embryology was published in the U.K.[1] The Committee, chaired by Dame Mary Warnock, was set up to consider ethical issues generated principally as a result of the success of Robert Edwards, Patrick Steptoe and Jean Purdy in their pioneering work on the fertilization of human oocytes *in vitro*, and the culture and replacement of these embryos with resulting pregnancy to term. Both the inspiration for this work, and the implications that flow from it, led the committee into wider areas of consideration including the provision of infertility services, the regulation of research on human gametes and embryos, and the regulation of certain forms of therapy for infertility, such as artificial insemination by donor (AID), egg and embryo donation and surrogacy. In this article we respond primarily to the proposals for regulating research, but first set these proposals in the general context of the report.

Human reproduction and embryonic development are sensitive issues. They are bound up with individual sexual identities, and thus permeate our whole social fabric. For this reason, discussion on the manipulation of reproduction is often emotive, dogmatic, and tinged with self- or group-interest. The Warnock Committee rightly sets the subject within a rational context – namely that at present the rights to reproduce and not to reproduce are not restricted in our Society, and therefore medical therapy that assists individuals in exercising these rights is as legitimate as any other medical therapy that enhances the well being and quality of life of the individual and of the family. The provision of a service for the infertile is as important as the provision of contraceptive advice. The Committee therefore recommend that a working group be set up at national level to draw up guidelines for such a service. This proposal is long overdue, should not be controversial and, if implemented, must become one of the most satisfying achievements for Edwards and his colleagues, who have for so long sought to draw attention to the present random, protracted and often ineffective approach to infertility treatment. In addition to being humane, this service will almost certainly save time and money for the Health Service. There is everything to recommend it.

The Committee's proposals for regulating the therapeutic use of *in vitro* fertilization, AID, egg donation and embryo donation are also sensible, based as they are on a sufficiently long period of practical experience to be obviously workable and fair. A licensing body is proposed that will regulate these services, and the unlicensed provision of these services will be an offence under the law. On the issue of surrogacy, the Committee takes a much harder line, recommending legislation to render illegal all surrogacy agreements undertaken by individuals and to render criminal all assistance given to individuals attempting to have children via the services of a surrogate mother. There are strong legal and medical reasons against this conclusion as put forward in a minority report from the committee itself and elsewhere subsequently.[2,3] We agree with these reservations, and feel that the committee was misguided on the issue of surrogacy which is best left to be regulated by the proposed Licensing Body.

Thus, with minor exceptions, the Committee has produced clear, sensible and practical proposals on the provision and regulation of infertility services. This clarity, sense and practicability seem all the more striking when one turns to the section of the report dealing with the regulation of research. On this aspect the Committee's report betrays a lack of attention to accurate detail and definition, a lack of awareness about the process of research itself, and a lack of trust in the scientific profession. If the proposals were to be implemented as presented, there is a real danger that all scientific and medical research on human fertilization and early embryogenesis would become so limited by uncertainty, as well as by regulation, as to cease.

Scientific Research and Its Regulation

Research, by its very nature, is pioneering and unpredictable. Its immediate value for medical application is often unclear, even to the majority of medical scientists themselves, until discoveries are made. Moreover, when discoveries do come work moves rapidly and needs to be pursued within a flexible framework. Good science will inevitably challenge existing values, and its apparent radicalism will often affront or disturb traditional ideas. A society that is eager to harness the benefits of science in the public interest must devise a regulatory framework that balances level-headed, non-partisan control against the inflexible stifling of science. Despite pointing this out themselves in para. 1.5 of the report, the Committee then proceeds to recommend proposals that do not strike this balance.

The Committee recommends both a